REMARKS

Claims 1-70 are in the case. The claims have been made subject to a requirement to restrict. Applicants have provisionally elected Group I containing Claims 1, 4, 6-11 and 14-47. Applicants hereby affirm that election. The affirmation of this election should not be construed as an endorsement of the examiner's rationale in making the election and Applicants reserve the right to file divisionals on non-elected claims.

Claims 2, 3, 5, 12, 13 and 48-70 are withdrawn from consideration. As the restriction has resulted in the separation of product and process claims and the possibility of rejoinder exists, Applicants are canceling no claims here and reserve the right to do so upon the allowance of the present application.

Claims 1, 4, 6-11 and 14-46 stand rejected variously under 35 USC § 112, 102 and 103. Claims 6, 7, 11 and 16-47 are objected to.

Claims 1, 7, and 31, have been amended to more clearly define Applicant's invention.

No new matter has been added. Amendments to the claims herein have not altered inventorship.

Claim Rejections – 35 USC § 112

Claims 7, 19-31, 40 and 42 are rejected under 35 USC § 112, second paragraph of indefiniteness.

Claim 7 is deemed indefinite because it is unclear how the analytical wavelength range is a window. It is unclear how the analytical wavelength is different from the optical wavelength. It is vague as to whether the analytical wavelength is within the range of the optical wavelength.

Applicants have amended the claim to remove the reference to "window". Analytical wavelength range is defined on page 24 (lines 20-31) of the specification. The optical wavelength range is defined on page 28 (lines 24-35) of the specification. It is clearly stated on page 28 (lines 26-27) that the analytical wavelength range is within the optical wavelength range. Thus, as described in the specification, the analytical range is any subset of wavelengths within the optical wavelength range where the subset may vary from about 1 to about 20 nanometers.

Claims 19-31 are deemed indefinite for the recitation of "substantially transparent". Applicants submit that the term is defined in the specification and is clear as used in the claim.

The phrase "substantially transparent" is defined on page 30 (lines 3-8) of the specification as meaning that "the absorption of light within the regions of the particle in which structural resonances are produced is sufficiently small so that when the particle is illuminated with light in the analytical wavelength range, the resonances remain observable".

Transparent to light over the analytical wavelength range means that the particle does not absorb light over the wavelength range used to scan the particle.

Claims 28 and 31 are deemed unclear because it is unclear if nanoparticles and colloidal particles are made from one of the materials listed or if the core/layer can be made of any material if it is a nanoparticle or colloidal particle.

Claim 28 is drawn to the core of the particle. The core may be comprised of colloidal particles. Claim 31 is drawn to layers on the microparticle. The layers of the microparticle may also be comprised of smaller colloidal particles. Applicants submit that the invention as claimed in Claims 28 and 31 is therefore clear and not indefinite.

Claim 40 is deemed to be unclear because it is not clear if capture probe is added or bound to the particle surface. The capture probe is fixed to the surface. The claim has been amended to empasize this limitation. Basis for this amendment is found on page 35 (lines 3-9) of the specification.

Claim 42 is deemed indefinite because it is unclear how the coating is activated. Additionally it is unclear if the coating prevents all binding or if it is specific for the capture probe. The specification describes activation of the coating. The activation of the coating to attach the capture probe involves chemical treatment and is described on page 42 (lines 1-10) of the specification and in Example 7. It is clearly stated in Claim 42 that the purpose of the film is "to prevent non-specific binding of the sample matrix components"; therefore, it is not specific for the capture probe.

Claim Rejections – 35 USC § 102

Claims 1, 4, 6, 8, 11, 16-23, 33,35 and 45-47 are rejected under 35 USC § 102(b) as being anticipated by Hansen (US 6200820), hereinafter "Hansen". Applicants respectfully traverse.

The method described by Hansen is significantly different than the resonant light scattering method of the instant invention. The method described by Hansen is an agglutination light scattering method wherein a first binding molecule-coated microsheres and second binding molecule-coated colloidal particles agglutinate in the presence of the analyte to form a complex. The non-colloidal particles, complexed and non-complexed, are detected using an optical flow particle analyzer in which the particles are counted by the light scatter pulse height caused by the particles passing through a flow cell. The measurement is made at a constant wavelength. The light scattering resonances that occur within each particle are not spectrally resolved. Rather, the statistical distribution of the light scattering signals for a population of particles, i.e., a histogram of the number of events versus the scattered pulse height (see Figures 2B, 2C, and 2D), is determined and correlated with the presence or amount of the analyte.

In the resonant light scattering method of the instant invention, the scattered resonances from each particle are resolved by scanning the particles over a wavelength range and recording the scattered intensity as a function of wavelength to obtain a resonant light

scattering signature or spectrum. Each particle can be identified based on its unique resonant light scattering signature and binding of a target analyte to each particle can be detected by a shift in wavelength of the resonant light scattering spectrum.

Applicants submit that the portions of Hansen that the examiner has chosen as teaching the various elements of the present invention do not describe these elements. For example, Col. 7, lines 10-23 describe a helium-neon laser or diode laser which produces light at discrete wavelengths and can not scan over an analytical wavelength range. Col 9 line 6-19, cited for the teaching that each particle is scanned for a first reference signature that identifies the particle, actually teaches the use of a discrete wavelength to indicate when several particles are immunocomplexed. This method does not assign a unique identifier to an individual particle.

A summary of the difference between Hansen and the claimed invention is given below:

1. Hansen do not teach the use of a light scanning source which produces light over an analytical wavelength range. The light sources described by Hansen., i.e., helium-neon laser or a laser diode, provide light at discrete wavelengths. They are not able to scan the particles over a range of wavelengths.

2. Hansen do not describe scanning each particle over a first analytical wavelength range to produce at least one first reference resonant light scattering signature for each particle. The method of Hansen uses a single wavelength of light. Thus a plot of scattered intensity versus wavelength, for each particle is not obtained and no unique resonant light scattering signature that differentiates one particle from another is obtained.

3. Hansen do not describe uniquely identifying each particle and correlating the capture probe with each identified particle. The method described by Hansen is not capable of uniquely identifying each particle. It can only identify a class of particles.

4. Hansen do not describe scanning the particles one or more times over a second analytical wavelength range to produce at least one second binding resonant light scattering signature. As described above, the method of Hansen does not involve scanning the particles over a range of wavelengths to obtain a resonant light scattering signature or spectrum.

5. Hansen do not describe detecting binding of at least one analyte to at least one capture probe by comparing the differences between the first and second resonant

light scattering signatures. In the instant invention, binding is detected by a shift in wavelength between the first and second resonant light scattering signatures or spectra for each particle. In the method of Hansen, binding is detected by determining changes in the statistical distribution of light scattering pulses for a population of particles.

6. Regarding Claims 19 and 20, Hansen do not describe a particle comprising a substantially spherical core and one or more layers overlaying the core, wherein the layers are substantially transparent to light over the analytical wavelength range. The particles of Hansen are not described as being substantially transparent to light. The colloidal particles used by Hansen are described as not scattering light in a manner which can be detected under the conditions used for the process (Col 7, lines 47-49). This statement means that the scattered light from the colloidal particles can be differentiated from that of the microspheres because their light scatter pulse height is significantly lower (see Figures 2B and 2C). The statement does not mean that the colloidal particles are substantially transparent to light (i.e., that they don't absorb light of the wavelength used).

In summary, Applicants submit that each and every element of the claimed invention is not found in Hansen and thus Hansen neither anticipates nor makes obvious the present invention.

Claim Rejections – 35 USC § 103

Claims 7, 9, 10, 14, 15, 24-28, 31 and 36-44 are rejected under 35 USC § 103(a) as being unpatentable over Hansen in view of West et al (US 6530944), hereinafter "West". Applicants respectfully traverse.

The teachings of Hansen are given above.

West is cited for the teaching that it is possible to scan a particle over an analytical wavelength range to obtain a shift in the wavelength of maximum resonance.

It is the Examiner's opinion that it would have been obvious to one of skill in the art to include in the method of Hansen the element of scanning a particle over an analytical wavelength range to derive the instant invention. Applicants respectfully traverse.

The discussion above relating to the differences between Hansen and the instant invention are relevant to this rejection and are incorporated here by reference. Applicants note that the Examiner has suggested in her arguments relating to the rejection under 35 USC § 102(b) that Hansen taught scanning the particle over an analytical wavelength (see page 7, section 13 of the present action). It would appear that if this limitation is already taught by Hansen, that the presence of such a limitation in West would not make the invention obvious.

Assuming for the moment however that scanning over an analytical wavelength is a new limitation added to the teachings of Hansen, it would still not render the invention obvious to the skilled person because of the l differences between the method of West and the present invention.

The method described by West is not resonant light scattering. It relates to surface plasmon resonance. West describes particles having a metal shell and a method of scanning the particles over an analytical wavelength range to obtain an absorption spectrum caused by the absorption of radiation by electrons in the metal shell, which forms electron waves (plasmons) within the metal. Therefore, the optical resonances described by West are not light scattering resonances. They are plasmon resonances. The differences in the method of West and the resonant light scattering method of the instant invention can be seen by comparing the spectra obtained by the two methods. The spectra shown by West (see for example figure 1) are plots of extinction (i.e.,absorption) as a function of wavelength and have peak widths of several hundred nanometers. The resonant light scattering spectra of the instant invention (see for example figure 9) are plots of the scattered light intensity versus wavelength and have peak widths of less than 1 nanometer. These are clearly not the same phenomena.

Additionally, the fact that Hansen do not teach the use of a first reference scan to uniquely identify an individual particle (Item 3 in Applicants summary of differences); and that a second scan of each individual particle is not performed to detect binding (Item 4 of Applicants' summary of differences) would mean that the combination of Hansen and West could not produce the elements of the claimed invention. The additional teachings of West in respect of claims 7, 14, and 15 (page 10 of the action) Claim 24 (Page 11 of the action); claims 25-28 (page 11 of the action); Claim 27 (page 12 of the action); and Claims 41-44 (page 12 of the action) are moot in view of the deficiencies in the teachings of Hansen.

Claim 29 is rejected under 35 USC § 103 (a) as being unpatentable over Hansen in view of Becker (US2003/0015428), hereinafter "Becker", and further in view of Hayashi (US5124207), hereinafter "Hayashi".

The teachings of Hansen are given above.

Becker is cited for teaching magnetic particles.

Hayashi is cited for teaching magnetic particles comprised of iron oxide.

It is the examiner's view that the skilled person would be motivated to apply the teachings of Becker and Hayashi with respect to magnetic particles to the methods of Hansen to derive the invention as set forth in claim 29. Applicants respectfully traverse.

Applicants arguments and comments in respect to the rejections under 35 USC § 102 and 103 above are relevant here and are hereby incorporated by reference. Claim 29 includes the limitation of a magnetic particle comprised of iron oxide. Applicants do not dispute that magnetic particles comprised of iron oxide are known however submit that, since Hansen

does not teach the limitations of the present invention that the combination of Becker, Hayashi, and Hansen would fail to put the skilled person in possession of the invention.

Claim 30 is rejected under 35 USC § 103(a) as being unpatentable over Hansen in view of Becker.

The teachings of Hansen and Becker are given above. Becker is additionally cited here as teaching a particle comprising a hollow core.

Claim 30 includes the limitation of a particle comprising a hollow core.

It is the Examiner's opinion that the teaching of Becker with respect to a particle comprising a hollow core, when combined with the method of Hansen would put the invention of Claim 30 in the possession of the person of skill in the art. Applicants traverse.

As argued above, Hansen does not teach the elements of the present invention. The teaching of a particle comprising a hollow core is not sufficient to counterbalance the deficiencies in the teaching of Hansen with respect to the present invention. Thus, Applicants submit that the invention is not obvious in view of the teachings of Hansen and Becker.

Claim 32 is rejected under 35 USC § 103(a) as being unpatentable over Hansen in view of Finlan (US 5055265), hereinafter "Finlan".

With respect to Claim 32 Hansen is cited for teaching a block made from high refractive index glass for the identification of an analyte where as Finlan is cited for teaching a glass block having a refractive index of about 2.

It is the Examiner's opinion that the teachings of Hansen when combined with Finlan suggest the claimed invention.

Applicants do not dispute the teaching of glass having a refractive index of about 2 however again submit that as Hansen does not teach the basic limitations of the present invention that the combination of Hansen and Finlan cannot make the invention obvious to the skilled person.

In view of the foregoing Applicants respectfully request reconsideration of the claims as amended and removal of all rejections.

Respectfully submitted,

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